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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,393	10/07/2003	Arthur G. Taveras	OC01643K1	5744

24265 7590 07/22/2005

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

SOLOLA, TAOFIQ A

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 07/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/680,393

Applicant(s)

TAVERAS ET AL.

Examiner

Taofiq A. Solola

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 24 June 2005.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-131 is/are pending in the application.
4a) Of the above claim(s) 74-131 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☐ Claim(s) 1-39 and 68-73 is/are rejected.
7) ☐ Claim(s) 40-67 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

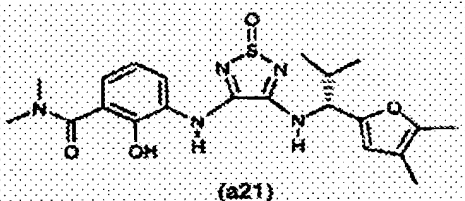
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Claims 1-131 are pending in this application.

Claims 74-131 are drawn to non-elected invention.

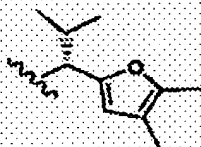
RESTRICTION REQUIREMENT

Applicant's election of group I, claims 1-73, with traverse in response to the Restriction Requirement is hereby acknowledged. The traversal is on the basis that in examining the compounds, the methods of use would be searched and vice versa, and that it would not be an undue burden to examine all the groups. This is not persuasive because it would constitute an undue burden to search all the groups for reasons set forth in the Restriction Requirement. In electing the invention of group I, applicant also elects the following compound

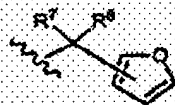


the following identification of substituent groups is made.

Substituent A is:



This A substituent is generically represented by the group



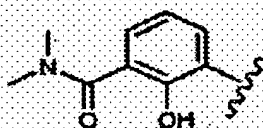
in paragraph (2) of the definition of the A substituents in Claim 1. This group can optionally be substituted with 1 to 6 substituents independently selected from the group consisting of R⁹.

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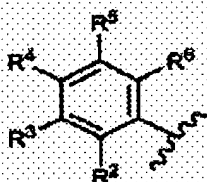
Thus, for Substituent A of the elected species:

one of R^7 and R^8 is H, and the other is unsubstituted alkyl,
wherein said alkyl is isopropyl, and
there are two R^9 substituents on the ring wherein each R^9 is an
 R^{13} group, and each R^{13} group is an unsubstituted alkyl, wherein said
alkyl is methyl.

Substituent B is



This B substituent is represented generically by the group:



in the definition of the B substituents in Claim 1.

Therefore, claims 1-73 are being examined in part subject to the election made by applicant.

Status of Claims

The Office has reviewed the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention encompasses all compounds within the scope of the claims, which fall into the same class and subclass as the elected compound, but may include additional compounds, which fall in related subclasses. Examination of the elected compound AND the entire scope of the invention encompassing the elected compound as defined by common classification results in the following:

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In formula I, A is a ring as defined in claim 1 but cannot directly attach to N. There must be an optionally substituted -CH₂- between ring A and N. Ring B is as defined in claim 1, but limited to those attached directly to N. R1-R40, g, and any other substituents are as defined in claim 1. As a result of the election and the corresponding scope of the invention identified herein, the remaining subject matter of claims 1-73 are withdrawn from further consideration by the Examiner, under 37 CFR § 1.142(b), as being drawn to a non-elected subject matter. The withdrawn compounds are patentably distinct from the examined invention as they differ in structure and element and would require a separate search. In addition, a reference, which anticipates the examined invention, would not render obvious the non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 37 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

"Salt" is defined in the specification, with such phraseologies as "Examples of such salts", line 3; "For example", line 8; and "Examples of suitable acids for salt", line 10. These imply the salts disclosed in the specification are examples. However, "Exemplification is not an explicit definition." Claim interpretation, 2004. The specification must set forth the definition explicitly and clearly, with reasonable clarity, deliberateness and precision, *Teleflex Inc. v.*

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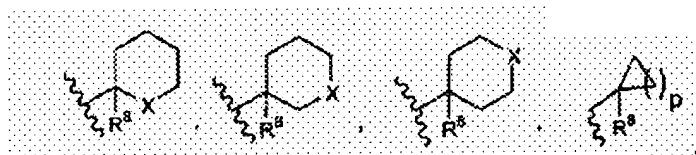
Ficosa North Am Corp., 63 USPQ2d 1374, (Fed. Cir. 2002). Rexnord Corp. v. Laitram Corp., 60 USPQ2d 1854 (Fed. Cir. 2001). By deleting the claim the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-39, 68-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 37 is indefinite for reasons set forth above under 35 USC 112, first paragraph.

In claim 1 several rings representing A and B are repeated. Therefore, claims 1-39, 68-73 are indefinite. For example, the following rings appear on pages 472 and 474.



The phraseologies "an unsubstituted heterocyclic acidic functional group . . . selected from the group consisting of: R₉ groups", claim 1, page 478, last 4 lines; "cycloalkyl groups wherein each alkyl group is independently selected," claim 1, page 479, lines 2-3; and "fluoroalkyl is one non-limiting example of an alkyl group that is substituted with halogen." Claim 1, page 481, lines 3-4, render the claim confusing and therefore claims 1-39, 68-73 are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 8, 29, 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Schostarez et al., Bioorg. Med. Chem. Letters, (1996), Vol. 6, No. 18, pages 2187-2192.

Schostarez et al., disclose compounds 8c-9r and 1 in Table 1. See also paragraph 1, page 2190.

Claims 1-2, 8, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Martinez et al., J. Heter. Chem. (1998), Vol. 35, pages 297-300.

Martinez et al., disclose compound 10 on page 298.

Allowable Subject Matter and Rejoinder of Claims

Claims 40-67 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The restriction of claims 74-131 is hereby withdrawn but would not be rejoined because of the following 35 USC, 112 problems. The claimed utilities are mere speculations, they are not believable, there is no such drug as one-size-fits-all as in the instantly claimed utilities, and the utilities are not supported by conclusive biological assays and/or published journal articles.

There is no evidence in the specification that the compounds are useful for treating all the forms of cancers known. The assays on pages 137-143 have no specific results, no discussion and/or explanation of the results and their relationship with each claimed utility. The following general

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statement, page 143, fails to establish any nexus between the compounds and any of the

There were compounds of this invention that had an EC₅₀ of <10 μ M. The compound of Example 2065 had an EC₅₀ of 13nM, the compound of Example 2066 had an EC₅₀ of 16nM, the compound of Example 2105 had an EC₅₀ of 3nM, and the compound of Example 2106 had an EC₅₀ of 12nM.

claimed utilities

The following statement, page 2, appears speculative and the specification fails to disclose how Arenber et al., demonstrate antitumor antibody for IL-8.

chemotaxis. Thus, these chemokines probably induce chemotaxis of endothelial cells toward their site of production in the tumor. This may be a critical step in the induction of angiogenesis by the tumor. Inhibitors of CXCR2 or dual inhibitors of CXCR2 and CXCR1 will inhibit the angiogenic activity of the ELRCXC chemokines and therefore block the growth of the tumor. This anti-tumor activity has been demonstrated for antibodies to IL-8 (Arenberg et al. 1996 J Clin Invest 97 p. 2792-2802), ENA-78 (Arenberg et al. 1998 J Clin Invest 102 p. 465-72), and GRO α (Haghnegahdar et al. J. Leukoc Biol 2000 67 p. 53-62).

The specification also cited several journals at the bottom of page 1 as implicating chemokines in a wide range of acute and chronic inflammatory disorders. However, these and other journals are not incorporated by reference in accordance with the MPEP, which states as follows:

A mere reference to another application, publication or patent is not an incorporation of anything therein into the application containing such reference for the purpose of satisfying the requirement of 35 USC 112, first paragraph. *In re de Seversky*, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). Particular attention should be directed to the subject matter and the specific portions of the referenced document where the subject matter being incorporated may be found. MPEP 608.01(p).

If the document is a pending US application: prior to allowance of an application that incorporates essential material by reference to a pending US application, if the referenced application has not been published or issued as a patent, applicant is required to amend the

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disclosure of the referencing application to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating the amendment consists of the same material incorporated by reference in the referencing application. MPEP 608.01(p).

Claim 68 is indefinite for failure to recite the structures of the compounds being claimed. Appropriate correction is required.

Claim 69 improperly depends from claim 1 for failure to limit the scope of claim 1. The compounds of claim 1 must be isolated and be pure to be applicable for their intended use. Also, there is no evidence in the specification that compounds of claim 1 are not isolated and in pure form. By deleting the claims the rejection would be overcome.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.


Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD. JD., whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (571) 273-8300.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.


T. A. Solola
Primary Examiner
Group 1626

July 19, 2005